

- 5     What is claimed is:
1.     A method of increasing insulin production, comprising contacting a pancreatic islet cell with a flavo-heme oxido-reductase polypeptide or an agonist thereof.
  - 10    2.     The method of claim 1, wherein said polypeptide comprises SEQ ID NO: 4.
  3.     The method of claim 2, wherein said polypeptide further comprises SEQ ID NO: 3.
  4.     The method of claim 2, wherein said polypeptide further comprises SEQ ID NO: 5.
  - 15    5.     The method of claim 1, wherein said polypeptide or agonist binds to a fatty acid.
  6.     A method of increasing insulin production, comprising contacting a pancreatic islet cell with a nucleic acid encoding a flavo-heme oxido-reductase polypeptide.
  - 20    7.     The method of claim 6, wherein said nucleic acid is operatively linked to a promoter, wherein said promoter directs expression of said nucleic acid preferentially in pancreatic islet cells compared to non-pancreatic cells.
  - 25    8.     The method of claim 7, wherein said promoter comprises a human insulin promoter.
  9.     A method of alleviating a symptom of diabetes in a subject, comprising administering to said subject a compound which increases the expression or activity of Ncb5or.
  - 30    10.    The method of claim 9, wherein said compound is a nucleic acid molecule encoding Ncb5or.
  11.    The method of claim 9, wherein said is an inducer of Ncb5or expression.
  - 35    12.    The method of claim 9, wherein said compound is a Ncb5or polypeptide.

13. A method of increasing insulin production in a cell, the method comprising contacting said cell with a composition which increases the expression or activity of Ncb5or.

14. The method of claim 13, wherein said cell is pancreatic cell.

15. The method of claim 13, wherein said cell is provided *in vivo*, *in vitro* or *ex vivo*.

16. A method of increasing serum insulin levels in a subject, the method comprising administering to said subject a compound which increases the expression or activity of Ncb5or.

17. The method of claim 16, wherein said compound is a nucleic acid molecule encoding Ncb5or.

18. The method of claim 16, wherein said is an inducer of Ncb5or expression.

19. The method of claim 16, wherein said compound is a Ncb5or polypeptide.

20. The method of claim 16, wherein the subject is suffering from or at risk of developing diabetes.

21. A method of decreasing serum glucose levels in a subject, the method comprising administering to said subject a compound which increases the expression or activity of Ncb5or.

22. The method of claim 21, wherein said compound is a nucleic acid molecule encoding Ncb5or.

23. The method of claim 21, wherein said is an inducer of Ncb5or expression.

24. The method of claim 21, wherein said compound is a Ncb5or polypeptide.

- 5    25.    The method of claim 21, wherein the subject is suffering from or at risk of developing diabetes.
- 10    26.    A method of diagnosing diabetes or a predisposition thereto, comprising detecting a mutation in a gene encoding Ncb5or, wherein the presence of said mutation indicates a diagnosis or diabetes or a predisposition thereto.
- 15    27.    A method of diagnosing diabetes or a predisposition thereto, comprising measuring the level of Ncb5or in a patient-derived bodily tissue, wherein a decrease in said level compared to a normal control level, indicates a diagnosis of diabetes or a predisposition thereto.
- 20    28.    A method of reducing white fat in a subject, comprising administering to said subject a compound which decreases the expression or activity of Ncb5or.
- 25    29.    The method of claim 28, wherein said compound is selected from the group consisting of a antisense Ncb5or nucleic acid, a Ncb5or-specific short-interfering RNA, and a a Ncb5or-specific ribozyme.
- 30    30.    The method of claim 28, wherein said compound is an inhibitor of oxidoreductase activity.
- 35    31.    A method of inhibiting the loss of beta cells in pancreatic islet tissue, comprising contacting said pancreatic islet tissue with a flavo-heme oxido-reductase polypeptide.
- 30    32.    The method of claim 31, wherein said pancreatic islet tissue comprises at least 10% more beta cells in the presence of said flavo-heme oxido-reductase polypeptide compared to the amount in the absence of said flavo-heme oxido-reductase polypeptide.
- 35    33.    The method of claim 31, wherein the amount of a reactive oxygen species in said pancreatic islet tissue is reduced in the presence of said flavo-heme oxido-reductase polypeptide compared to the amount in the absence of said flavo-heme oxido-reductase polypeptide.

34. The method of claim 33, herein said reactive oxygen species comprises superoxide ( $O_2^-$ ) or ferri-heme.
35. The method of claim 31, further comprising contacting said pancreatic islet tissue with a  
10 anti-oxidant.
36. The method of claim 35, wherein said anti-oxidant is a niacin compound.
37. The method of claim 36, wherein said niacin compound is nicotinamide.  
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38. A method of increasing the viability of primary pancreatic islet cells, comprising  
contacting said islet cells ex vivo with a flavo-heme oxido-reductase polypeptide or agonist  
thereof.
- 20 39. A method of increasing the viability of transplanted donor pancreatic islet cells in a  
transplant recipient, comprising administering to said transplant recipient a flavo-heme oxido-  
reductase polypeptide or agonist thereof.
- 25 40. The method of claim 39, wherein said polypeptide or agonist thereof is administered  
locally to a transplantation site.
41. The method of claim 39, wherein said polypeptide or agonist thereof is administered  
systemically.
- 30 42. The method of claim 39, wherein said polypeptide or agonist thereof is administered prior  
to transplantation of said donor pancreatic islet cells.
43. The method of 39, wherein said polypeptide or agonist thereof is after transplantation of  
said donor pancreatic islet cells.  
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- 5       44. The method of 39, wherein said polypeptide or agonist thereof is administered concurrently with transplantation of said donor pancreatic islet cells.
- 10      45. A method of inhibiting cell death, comprising contacting a cell with a composition comprising a flavo-heme oxido-reductase polypeptide or an agonist thereof.
- 15      46. The method of claim 45, wherein said polypeptide comprises SEQ ID NO: 4.
- 20      47. The method of claim 45, wherein said polypeptide further comprises SEQ ID NO: 3.
- 25      48. The method of claim 45, wherein said polypeptide further comprises SEQ ID NO: 5.
- 30      49. The method of claim 45, wherein said cell is a pancreatic cell.
- 35      50. The method of claim 49, wherein said pancreatic cell is a  $\beta$ -cell.
- 40      51. The method of claim 45, wherein said cell is provided *in vivo*, *in vitro* or *ex vivo*.
- 45      52. The method of claim 45, wherein said cell death is oxidative stress induced cell death.
- 50      53. The method of claim 45, wherein said cell death is apoptotic cell death.
- 55      54. A pharmaceutical composition comprising a Ncb5or polypeptide.
- 60      55. The composition of claim 54, wherein said composition further comprises a fatty acid.
- 65      56. A pharmaceutical composition comprising a Ncb5or nucleic acid.
- 70      57. A method of identifying an agent that increases insulin production, comprising:

5 (a) contacting a cell comprising a Ncb5or polypeptide with a test agent; and

(b) determining the level of oxidase activity in said cell, wherein an increase in oxidase activity in the presence of said agent compared to said level in the absence of said agent indicates that said agent increases insulin production.

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58. A method of identifying an agent that decreases fat accumulation, comprising:

- (a) contacting a cell comprising a Ncb5or polypeptide with a test agent; and
- (b) determining the level of oxidase activity in said cell, wherein an increase in oxidase activity in the presence of said agent compared to said level in the absence of said agent indicates that said agent decreases fat accumulation.

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59. A transgenic mouse comprising comprising a homozygous disruption in a *Ncb5or* gene.

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